ABSTRACT OF THE DISCLOSURE

The invention relates to modified oligonucleotides that are useful for studies of gene expression and for the antisense therapeutic approach. The invention provides modified oligonucleotides that inhibit gene expression and that produce fewer side effects than conventional phosphorothioate oligonucleotides. In particular, the invention provides modified CpG-containing oligonucleotides that result in reduced splenomegaly and platelet depletion when administered to a mammal, relative to conventional CpG-containing phosphorothioate oligonucleotides. The invention further provides methods for using such oligonucleotides to modulate gene expression *in vivo*, including such use for therapeutic treatment of diseases caused by aberrant gene expression.